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REVIEW ARTICLE

Locally Recurrent Rectal Cancer: Role of Composite Resection of Extensive Pelvic Tumors With Strategies for Minimizing Risk of Recurrence

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Locally recurrent cancer of the rectum has been under-recognized as a complication, although it affects up to 40% of patients treated with surgery alone. Even in the best centers, rates average 25%. While radiotherapy may reduce recurrence, it is now apparent that total mesorectal excision is the most effective modality, with rates as low as 5%. The dramatic decrease in local recurrence can also be linked to increased survival in prospective studies, an effect more significant than any adjuvant therapy. The options, however, for patients with locally recurrent cancer are limited. Fifteen percent of patients with this complication die without systemic spread. Salvage by surgery offers potential cure. Other than anastomotic recurrences that can be locally resected, the best approach for long-term survival is an extensive surgical procedure requiring en bloc removal of adjacent organs and pelvic structures—so-called composite resection. With careful selection, 30% 5-year survival can be achieved and palliation is considerable, with 50% long-term local control. Intraoperative radiotherapy and brachytherapy, and/or preoperative chemoradiation may provide better results in future. Newer techniques of coloanal anastomosis, improved urinary diversion, and myocutaneous flaps for perineal reconstruction radically reduce the morbidity of these procedures. The approach to recurrent rectal cancer requires a sophisticated multidisciplinary team to obtain optimum results.
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KEY WORDS: recurrent rectal cancer; composite resection; total mesorectal excision

INTRODUCTION

Locally extensive pelvic cancer, whether primary or recurrent, is one of the most challenging problems in oncology. Often patients who present with locally advanced disease are only offered palliative treatment—radiation or a defunctioning colostomy. Consequently, they go on to suffer a lingering, miserable deterioration, with progressive symptoms that may include pain, bleeding, intestinal or urinary fistulae, and obstruction. Treatment is either ineffectual or offers only a brief hiatus in their relentless downhill course. Death must seem a welcome release from such terrible suffering. Unfortunately, this problem is not a rare one. Primary cancers of the rectum, cervix, and prostate all have the potential to in-

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vade adjacent pelvic structures, and recurrent disease is even more likely to be locally extensive. In rectal cancer, which has provided most of our experience with the surgical management of this problem, almost 30% of patients who undergo a curative operation for their primary cancer will relapse locally [1]. Because it is such a devastating problem, local recurrence challenges us, as surgeons and oncologists, to re-evaluate all aspects of the primary treatment of these cancers. Better surgical techniques, adjuvant radiotherapy and chemotherapy, and enhanced surveillance for recurrent disease all have potential to reduce the terrible morbidity and mortality associated with this problem. In our opinion, optimal initial treatment, though it might appear radical, is far preferable to the inexorable progression of residual or recurrent pelvic cancer. In this article, we will explore the whole problem of locally recurrent rectal carcinoma, factors that predispose to relapse in the pelvis, means of preventing it, and, finally, strategies for treatment.

INCIDENCE AND PREDICTORS OF LOCAL RECURRENCE

Several large reviews of outcome have identified an overall recurrence rate of >40% in rectal cancer, with pelvic recurrence the most common first site of relapse [2]. Among patients who relapse locally, half have isolated pelvic failure [3,4], suggesting that better local control has significant potential to improve cure rates. Two studies of patterns of recurrence in rectal cancer have demonstrated that local failure, without clinical evidence of distant metastases, accounts for about half the cancer-related deaths at 5 years. In a large series, reported by McDermott et al. [5], 27% of rectal cancer deaths were attributable to isolated local relapse, and another 24% had combined local and systemic failure. Perhaps the best documentation of this pattern of disease behavior is an autopsy series reported by Welch and Donaldson [6]. Not surprisingly, they discovered a much higher incidence of local recurrence at necropsy than was diagnosed clinically in patients who died of rectal cancer. In that report, 25% of patients had only local disease at the time of death, 50% had both local and systemic disease, and only 25% died of systemic metastases alone. It is clear that local recurrence is common, and a significant contributor to mortality from rectal cancer.

Several tumor characteristics have been consistently identified as predictors of disease recurrence. Without doubt, lymph node involvement and full thickness penetration of the muscular wall of the rectum are the most influential factors; thus risk increases significantly with advancing T or N stage [7–14]. While other pathologic features of the primary tumor have been implicated (including microvascular and perineural invasion [12], tumor grade, and morphology [15]), their importance is overshadowed by depth of invasion and nodal status. There is some evidence that more distal tumors recur more frequently than those in the proximal rectum. McDermott et al. [5] found a local recurrence rate of 14% for upper third tumors, 21% for middle, and 26% for lower third tumors. Perhaps this variation is partly explained by the anatomic constraints of surgery in the pelvis, which make it difficult to obtain adequate clearance around low rectal lesions.

SURGICAL TECHNIQUE AND LOCAL RECURRENCE

Many reports during the 1970s and 1980s focused on the relationship between local recurrence and technical aspects of surgery, such as the length of the distal resection margin, preservation of the anal sphincter, high ligation of vascular and lymphatic pedicles, and even deep iliac node dissection. None of these showed a convincing association with local recurrence. Several studies have demonstrated that distal intramural spread of rectal cancer is unusual beyond 1 cm, and extremely rare beyond 2 cm [16,17]. Involved pararectal lymph nodes are also confined within a 2 cm distal margin, even in high-grade, infiltrative tumors [18]. Retrospective analysis of clinical outcome indicates that neither survival nor local recurrence correlates with distal clearance, provided a 2 cm margin is maintained. The issue of the safety of sphincter-saving resections for low rectal cancer remains somewhat troublesome. The British Large Bowel Cancer Project [9] found a higher local recurrence rate (18%) after anterior resection, than after abdominoperineal resection (12%, $P < 0.02$), as did the National Surgical Adjuvant Breast and Bowel Project R-01[19], whereas many other, smaller studies [5,13,15,20,21] have found no significant difference in local failure rates between the two procedures.

More recently, attention has turned to surgeon-related variation in outcomes. The British Large Bowel Cancer Project [9], a multicenter trial involving 93 surgeons, identified surgical technique as an important determinant of local recurrence. In that study, local relapse rates varied from less than 5% to greater than 20% among different consultants. Experience, by itself, did not appear to be a factor, as operations performed by "junior staff" were no more likely to produce local recurrence than those performed by consultants. A recent study comparing local recurrence rates after rectal cancer resection in a group of surgeons in Alberta, Canada [22] showed that local recurrence and disease-free survival were affected by the surgeon's level of training and experience in colorectal surgery, as compared with general surgeons whose practice included fewer of these operations. In fact, the findings were quite dramatic. Patients of surgeons who had additional training or expertise in colorectal surgery had a local relapse rate of 13%, compared with 34% among patients of general surgeons ($P = 0.001$).

Even though it is clear that the quality of surgery strongly affects local recurrence in rectal cancer, the reason for this remained obscure until recently. It now seems that the crucial factor is the status of the lateral or circumferential margin of resection, which is determined both by the biologic behavior of the cancer, and by the technique of the surgeon. The first convincing report to implicate the circumferential margin as a source of residual cancer was that of Chan et al. [23], published in 1985. They examined whole-mount sections of 50 rectal cancers, and applied a standardized method of measuring radial surgical clearance. Seven of the 50 specimens had tumor at the radial resection margin, although the operations were thought curative when examined using standard histopathologic sections. Although this descriptive study made no association between radial margin status and local recurrence risk, a prospective study by Quirke [24] the following year established that link. Quirke's method was intensive and time-consuming. The entire tumor was embedded and examined in serial transverse sections. Using this method, he identified positive radial margins in 14 of 52 cases, which predicted local recurrence in 12 of 14 (85%).

For comparison, a cohort of patients matched for Dukes stage and histologic grade, whose standard pathologic examination indicated clear margins, was also analyzed. They had a similar local recurrence rate of 27%, despite having negative margins with standard pathologic analysis. Later, Adam et al. [25] reported a larger, prospective study correlating radial margin status with outcome. Among 190 patients who underwent curative resection of rectal cancer, the rate of circumferential margin involvement was 25%, and a positive margin proved strongly predictive of local relapse. Among those with clear margins, 90% remained free of pelvic recurrence at 5 years, whereas only 23% of those with lateral margin involvement were without local recurrence. In multivariate analysis, circumferential margin involvement was the most powerful predictor of local recurrence (hazard ratio 12.2) and of overall cancer mortality (hazard ratio 3.2).

TOTAL MESORECTAL EXCISION

In parallel with these studies by Quirke and others, Heald and colleagues [26–30] perceived that the radial resection margin was a critical component in the surgical approach to rectal cancer. Based on the premise that the extrarectal spread of tumor occurs in a centrifugal pattern, and often remains confined to the mesorectum, even in stage III disease, Heald developed a method of resection in which the mesorectum is completely excised, in continuity with the tumor-bearing segment of bowel. This operation was christened "total mesorectal excision" (TME). Briefly, TME consists of meticulous, sharp dissection between the visceral mesentery of the rectum and the parietal fascia of the pelvic wall, the sacrum posteriorly, and the bladder and prostate or vagina anteriorly. Laterally, it is important to identify the pelvic autonomic nerve plexus, which lies along the pelvic sidewall and surrounds the middle rectal artery. By careful preservation of these nerves, with deliberate sacrifice of those which enter the mesorectum to supply the rectum, normal sexual function can be preserved in 85% of patients [31]. Bladder function is also preserved in virtually all cases. Anteriorly, the dissection proceeds in front of Denonvillier's fascia, which is incised where it merges with the prostatic capsule in the male. Caudally, mesorectal excision extends to the pelvic floor, exposing most of the levator musculature, and clearing the distal rectal tube of its enveloping fatty tissue. This precise, extensive dissection results in removal of the whole mesorectum, which Heald describes as the intact "tumor package." In doing so, it preserves autonomic nerve function, but the risk of anastomotic leakage from the partially devascularized rectal stump is increased. Clinically, Karanjia et al. [32] and Heald [33] report an anastomotic leak rate of 11%, and Enker et al. [31], using TME, reports leaks in 3% [31]; a diverting stoma (ileostomy or transverse loop colostomy) has been advocated to prevent this complication.

In terms of cancer outcomes, Heald's results are impressive. Using TME, without adjuvant radiation, he reports a local recurrence rate of 4% at 10 years in patients undergoing curative surgery for rectal cancer [27]. Among high risk cases (Astler-Coller B2 and C stages), local recurrence at 5 years was 5%, and disease-free, cancer-specific survival was 78%. The latter results are directly comparable to those of the North Central Cancer Treatment Group (NCCTG), which included prestigious US institutions and surgeons. That study [34] yielded a local recurrence rate of 25% in the control arm, where patients received standard surgery plus adjuvant postoperative radiation; this local failure rate was reduced to 13.5% by adding chemotherapy to the postoperative treatment regime. Similarly, the chemoradiation group also had improved rates of overall disease recurrence—42% versus 63% at 5 years. Although it is clear that adjuvant therapy can improve outcomes in rectal cancer, the results of Heald's operation remain better than the best reported results of multi-modality therapy. Nor are Heald's results idiosyncratic; similar outcomes have been reproduced by Enker et al. [31] using TME at Memorial Sloan-Kettering Cancer Center in New York City. In their reported series of 240 consecutive patients undergoing total mesorectal excision for Dukes B and C rectal cancers, the rate of pelvic recurrence was only 7.8%, with a 74% 5-year survival rate. Many surgeons in Europe, Scandinavia and North America have now acquired Heald's technique through a program of preceptored teaching, and its superiority over standard rectal

resection is presently being validated in multicenter trials.

ADJUVANT RADIOTHERAPY

The role of radiotherapy in achieving local control also deserves close consideration, since a number of studies have shown its efficacy. Preoperative radiation appears to be more effective than postoperative treatment, although it precludes accurate pathologic staging, and means that a certain number of early stage cancers will be unnecessarily included. Improved preoperative assessment of T-stage using endorectal ultrasound may help to avoid overtreatment of lesions that do not penetrate the full thickness of the muscular wall of the bowel. A randomized multicenter Swedish trial [35] compared preoperative short-term, high dose radiotherapy (25.5 Gy in 1 week) to conventional postoperative radiation (60 Gy in 7–8 weeks) in those with Dukes B and C lesions. The local recurrence rate was lower in the preoperatively irradiated group (13% versus 22%, $P = 0.02$), and survival was also superior by 10% ($P = 0.004$) [70]. There are also several reports of improved survival, as well as lower local relapse rates, when preoperative radiation is compared with no adjuvant treatment. A 1988 European Organization for Research and Treatment of Cancer (EORTC) report [36] noted that preoperative radiotherapy reduced local failure from 30% to 14% at 5 years, without having any impact on survival. The results of the Stockholm I trial [37] were almost identical, in terms of local recurrence. However, a surplus of deaths due to cardiovascular or infectious complications among radiated patients in the early postoperative period canceled their advantage in cancer-specific survival, so that no difference in overall survival was seen. Postoperative radiation, by itself, has not shown promising results in either local control or survival, and it appears to be associated with more complications than preoperative radiotherapy [38]. Only in conjunction with chemotherapy, as in the NCCTG trial [34] mentioned above, has postoperative radiation produced improvement in local control. In that case, a benefit in disease-free survival was also observed.

SURVEILLANCE STRATEGIES

Currently, "acceptable" local recurrence rates after curative surgery for rectal cancer range around 20%. We can expect considerable improvement in local control with the increasing prevalence of precise surgery, encompassing the entire mesorectum, and the appropriate use of preoperative radiotherapy or chemoradiation. Nonetheless, local recurrence is likely to remain a serious problem in this disease. The role of systematic surveillance in picking up pelvic recurrence at an asymptomatic stage is controversial, and whether "early detection" of isolated local failure improves cure rates is open to question [39]. A prospective trial by Schiessel et al. [40] suggests that it might. Using a regime of regular physical and endoscopic evaluation, along with carcinoembryonic antigen (CEA) assays, they detected half of all local recurrences at an asymptomatic stage. This contrasts with most other series, in which 90% of patients are symptomatic. Analysis of local recurrence in the Stockholm Rectal Cancer Trial [41], for instance, revealed that pain was the dominant symptom (62%), followed by disturbances in micturition (26%), rectal or vaginal bleeding (18%), altered bowel habit (14%), rectal or vaginal discharge (11%), fistula (7%), ileus (5%) and uremia (4%). In that trial, only 17% of patients who underwent reoperation were able to have their tumor completely removed, macroscopically. This suggests that the presence of symptoms is an indicator of more advanced disease. By contrast, in Schiessel's study, 42% were able to undergo radical reoperation resulting in microscopically clear margins. Median survival in this group was 17 months, and 30% were still living at 3 years follow-up.

Newer modalities such as endorectal ultrasound and radio-immunoscanning have been suggested as better means of identifying pelvic recurrence, but none has yet achieved the sensitivity or specificity of the computed tomography (CT) scan [42,43]. Lately positron emission tomography has shown promise in this area [44], but it continues to be expensive and not widely available. Other tumor markers such as tissue plasminogen activator and CA 19-9 have been used in conjunction with CEA to improve pick-up of recurrent disease [45]. A rising CEA level is certainly an indication for more intensive work-up, including CT scanning of lungs, abdomen, and pelvis; unfortunately, CEA often remains normal in the presence of isolated pelvic recurrence. Even with the imminent availability of more sensitive tests, the question of whether intensive follow-up for local recurrence can ultimately affect survival remains to be answered.

COMPOSITE SACROPELVIC RESECTION

Surveillance for pelvic recurrence only makes sense if it is coupled with a policy of aggressive reoperation or other treatment. In rectal cancer, relapse in the pelvis is commonly associated with extension to adjacent organs, and sometimes to the pelvic sidewalls, or to the sacrum posteriorly. In keeping with established principles of cancer surgery, the recurrent tumor must be excised en bloc, in continuity with all the involved structures, if local control or cure is to be achieved. This type of operation, if it involves portions of the bony pelvis, has been called "composite resection" or alternatively, "sacropelvic resection." Although in most centers, patients with fixed pelvic recurrence are considered suitable only for palliative treatment, our experience, and recent published work by several other surgeons, indicates that composite resection is a reasonable option for appropriately selected

patients. In the remainder of this article, we will define criteria for selection of patients for this procedure, explain the surgical technique in some detail, and review the results of composite resection of recurrent rectal cancer.

OPERATIVE CRITERIA

First of all, patients who present with local recurrence must be assessed not only in reference to the local extent of their disease, but for the possibility of systemic spread. Whole body CT scanning is essential to exclude cranial, pulmonary, and hepatic metastases, as well as para-aortic and iliac lymphadenopathy, and other sites of intra-abdominal disease. We also routinely perform a bone scan, as many of these patients present with complaints of musculoskeletal or radicular pain, and osseous metastases should be sought. The presence of extrapelvic disease is generally accepted as a contraindication to curative resection. Once systemic or regional disease has been ruled out, the local encroachment of the tumor on adjacent bony, vascular, and visceral structures must be ascertained. If direct bony invasion is suspected, radiographs of the involved structures should be obtained. Magnetic resonance imaging (MRI) and bone scans will also help to answer this question. A positive result, indicating that the tumor has penetrated the cortex of bone to invade the marrow, eliminates the possibility of curative resection. A further criterion of inoperability has been identified by Rodrigues-Bigas et al. [46], who noted that all patients whose recurrent rectal cancer was associated with unilateral or bilateral hydronephrosis, had unresectable disease. We also concur with other authors who have listed sciatic nerve pain [47], a frozen pelvis [48], and unilateral leg edema [48] as preoperative contraindications to resection.

The importance of factors such as tumor growth rate and the rapidity of recurrence after primary treatment are less well documented in relation to either operability or survival after re-resection. It is our impression, however, that prompt recurrence after adequate initial treatment contraindicates exenteration. On the other hand, an early recurrence after less radical surgery may have a different prognosis. On average, two-thirds of patients with pelvic relapse after simple local excision of their tumor are able to undergo curative re-excision, whereas for more radical primary surgery, complete re-excision is usually possible in only 30% [49]. Low anterior resection also appears to result in a small number of central, anastomotic recurrences that are easy to detect and treat. Unfortunately, these relatively favorable lesions comprise only 25% of locoregional relapses after anterior resection [49]. Most appear to arise in the residual mesorectum, and encroach on the lumen only secondarily, at a more advanced stage of their growth. Abdominoperineal resection (APR), the most extensive of the standard operations for rectal cancer, is apt to relapse with diffuse pelvic tumor or laterally situated masses invading the pelvic sidewall. Therefore, recurrence after APR has, in general, a poorer prognosis [49,50].

Taking these criteria into account, along with the overall health and cardiorespiratory status of the patient, a decision may be made to offer re-operation. At that point, a thorough discussion of the procedure and its attendant morbidity must take place, so that the patient clearly understands the risks of operation and its consequences. The impact of sacropelvic resection on all facets of a patient's life is tremendous. Sexual function is severely affected, the bladder is usually replaced by an ileal conduit, and a colostomy is required. Even ambulation may be affected, if a high sacral resection is undertaken. If these issues are not seriously considered preoperatively, an emotional and functional disaster will almost surely ensue.

HISTORICAL DEVELOPMENT

Pelvic exenteration was first described by Alexander Brunschwig in a 1948 report [51] that included mainly patients with advanced primary and recurrent cervical cancer. It was not until 1969 that Brunschwig and Barber [52] published the first series of composite sacropelvic resections, in which they described 9 cases of "pelvic exenteration combined with resection of segments of bony pelvis." None was cured, although 2 patients survived >5 years with residual or recurrent rectal cancer. While Brunschwig may be credited with the inception of composite resection, the procedure was really developed and championed by Wanebo and Marcove [53]. Following the publication of their pioneering work in 1981, composite resection could be considered as a reasonable alternative to palliative radiation, which was formerly the standard therapy for recurrent rectal cancer with sacral fixation. The principles of composite resection are really no different than those that apply to standard pelvic exenteration for locally advanced cervical or rectal cancer. Therefore, it is not too surprising that Wanebo et al. [1] reported long-term survival of 20–30% in patients undergoing composite resection, results very similar to those obtained with pelvic exenteration. Their experience remains the largest series of composite resections, with the most extensive follow-up. We will consider the updated results of his work after examining the technique itself, as Wanebo described it.

SURGICAL TECHNIQUE AND RESULTS OF COMPOSITE RESECTION

There are, in fact, two surgical approaches to sacropelvic resection. The operation practiced by Wanebo is a 2-stage procedure, which begins with an anterior approach, followed, at an interval of 1 or 2 days, by the posterior, sacral operation. An alternative, which we pre-

fer, is the 1-stage operation, done in lithotomy position. The 2-stage operation is concisely outlined and beautifully illustrated in several publications by Wanebo and colleagues [53,54]. In the first part of the operation, a laparotomy is carried out, with meticulous search of the abdomen, looking for extrapelvic disease. Liver metastases, serosal seeding or para-aortic nodal metastases are considered contraindications to curative resection. Dissection is then begun along the lower aorta and iliac arteries. An assessment is made of the pelvic lymph nodes. If they are extensively involved with tumor, the procedure should be terminated; if not, a formal pelvic lymph node dissection should be done, including the obturator nodes. If the tumor invades bladder or ureters, an ileal conduit is constructed. Otherwise, the ureters should be moved anterolaterally to place them out of harm's way during the transection of the sacrum via the posterior approach. Ligation of the vascular supply includes division of the internal iliac arteries and veins, as well as the middle sacral artery and veins. Finally, a sigmoid end colostomy is done, leaving the stapled stump of rectum in place, attached to the sacrum. The abdomen is then closed and the patient placed in the prone position for the posterior, sacral resection.

During this second part of the operation, a midline incision is made over the sacrum, curving inferolaterally around the buttocks bilaterally. Subcutaneous flaps are created, exposing the gluteus maximus. By splitting this muscle, one can identify the sciatic nerve. The gluteal muscles are then dissected off the sacrum, and the sacrotuberous and sacrospinous ligaments are incised at their respective attachments to the ischium. The surgeon can then insert his or her finger through the endopelvic fascia below and medial to the pyriformis muscle and the sciatic nerve. This allows palpation of the pelvic floor and assessment of the level of resection. The patient's prone position now makes it possible to perform a sacral laminectomy just above the planned level of resection. This maneuver enables one to ligate the end of the dural sac and to preserve the proximal sacral nerve roots under direct vision. It is especially important to avoid injury to the S1 nerve roots; if they are transected, loss of plantar flexion will result [55]. Bilateral transection of S2 nerve roots compromises bladder function, producing poor detrusor tone and increased residuals; bilateral transection of S1 results in complete denervation of the bladder [55]. After the resection line has been determined on both sides of the sacrum, an osteotome or oscillating saw is used to transect the sacrum, again using a finger in the pelvis to guide the osteotomy. Above S2, the line of resection must include part of the sacroiliac joint; however, even for sacral resection at the mid-body of S1, the stability of the pelvic ring is maintained. Finally, the sacrum, pelvic sidewalls, and tumor are removed en bloc, along with the attached visceral structures previously mobilized. The wound is packed temporarily to control bleeding, which is most profuse at this stage of the procedure. After hemostasis is obtained, the pelvic defect is reconstructed with local gluteus flaps, or distant myocutaneous flaps.

Turk and Wanebo [55] and Wanebo et al. [56] report a mean operative blood loss of 10 liters and a mean operating time of 18.5 h for this 2-stage procedure. Two to 3 days were sometimes required to stabilize the patient between the abdominal and sacral parts of the operation. Reflecting the magnitude of the operation, surgical mortality in this series was 8.5%. Major morbidity included cardiopulmonary insufficiency, postoperative hemorrhage, and intestinal fistulization, each occurring in about 20% of patients. Serious wound complications occurred in 25%. Despite all this, most patients felt their quality of life was improved by the surgery [55].

Before proceeding to an analysis of long-term results in Wanebo's series, we will describe the alternate, 1-stage operation which we generally use. In most key respects, this procedure is similar to what has just been described. The difference centers on the use of a combined abdominal and perineal approach, carried out with the patient in lithotomy position, with a pad placed under the lower lumbar spine to elevate the sacrum off the operating table. Our initial approach of staging and mobilizing the tumor and pelvic organs is identical to Wanebo's. The principle of resection is to maintain a margin of 1 cm, or one tissue plane, beyond the cancer. Mobilization along the pelvic sidewall takes place in the plane of the endopelvic fascia. The pelvic nodes are included with the tumor excision, and when soft tissue invasion is noted, the involved fascia and muscles, including the obturator internis and pyriformis, may be resected to obtain clear margins. In any area where there is suspicion of residual disease, it is important to obtain frozen section pathology, to verify a microscopically complete resection. The branches of the lumbosacral trunk are preserved, unless directly invaded by tumor. S1 and S2 are important in maintaining function of the leg, while adequate bladder function can be obtained by preserving S2 and S3 on one side. Throughout the mobilization of the tumor, one works to free the anterior and lateral margins of resection, but no attempt is made to separate the mass from the sacrum posteriorly. Instead, the sacrum is cleared for transection 1–2 cm above the proximal edge of the adherent tumor.

The perineal excision is begun only when the entire specimen has been freed completely anterolaterally, and the anterior cortex of the sacrum exposed at the level of transection. To prevent excessive bleeding during transection, we have found it extremely useful to temporarily cross-clamp the aorta above its bifurcation. This maneuver has cut average blood loss in half. During the perineal excision a margin of 2.5–3 cm is maintained around the

TABLE I. Results of Selected Series of Sacropelvic Resection for Recurrent Rectal Cancer

Reference	Year	No. of patients	Local relapse	Alive[a]	
				With disease	Without disease
Brunschwig and Barber [52]	1969	9	4 hospital deaths, 5 dead of disease at 11–72 mo		
Sugarbaker et al. [58]	1982	6	0	—	4 patients >3 yr
Takagi and colleagues [59]	1986	7	2	2	2 (3, 22 mo)
Pearlman et al. [60,61]	1987	12	4	1	3 (6–48 mo)
Touran et al. [62]	1990	12	5	4 (1 yr)	
Maetani and colleagues [63]	1992	23/33		3 (5 yr)	1 (5 yr)
Temple and Ketcham [57]	1992	20	50%		2 (12, 15 yr)
Wanebo et al. [1,53–56]	1994	47	13	1 (5 yr)	10 (5 yr)
Sardi et al. [64]	1994	3/6	3	5 (9–37 mo)	0
Wiggers et al. [65]	1996	6/23	60%	1	9 (20%, 5-yr Kaplan-Meier)
Magrini et al. [66]	1996	16	3	2	7 (2–37 mo)

[a]yr = year(s), mo = month(s).

tumor in all directions. The attachments of the gluteus maximus to the sacrum are divided up to the intended level of transection, and an osteotome is then used to sharply and quickly transect the sacrum. Heavy curved Mayo scissors are used to divide any remaining soft tissue attachments, and the specimen is then removed. To obtain an adequate margin laterally, the ischial tuberosity may be excised, and anteriorly, the pubis may be removed as necessary. In fact, we have sometimes found it helpful to split the pubic symphysis to improve access to the deep pelvis in cases where there is uncontrolled bleeding. Once the specimen is removed, however, it becomes easier to see and oversew any large bleeding vessels. It is important to check for leaking cerebrospinal fluid at this point, as well as to free the cauda equina and repair any defect in the dural sac. An ileal conduit or continent pouch is created for patients who have had a concurrent bladder resection, and a colostomy is constructed.

Closure of the large pelvic defect that remains after sacropelvic resection is a challenging problem. Omentum is helpful, but frequently it is inadequate, or has been destroyed by previous surgery. We have experimented with many types of flap closure, including the gluteus maximus and the gracilis and tensor fascia lata and have found the rectus abdominis flap the most reliable and versatile. Its abdominal origin eliminates the problem of anchoring the flap in the pelvis, and, in women, the skin paddle can easily be tubularized to create a neovagina. If the patient requires both a colostomy and a urinary stoma, we prefer to use rectus muscle from the side of the urinary conduit. Our choice of urinary diversion has generally been the Indiana pouch, rather than the standard ileal conduit.

With this 1-stage approach, the mean operating time is 8 h, and median blood loss 9 units. Cross-clamping the aorta has reduced the mean blood loss from 10 units to 5. Our hospital mortality for this procedure is 10%. Morbidity has included bowel or ileal loop leaks in 15% and breakdown and secondary healing of the perineal incision in 30%. Since we began using rectus myocutaneous flaps for reconstruction, the wound complication rate has dropped quite dramatically to 12% [57].

It is evident that sacropelvic resection is technically feasible, although difficult. Operative mortality, in experienced hands, is between 8 and 10%, and serious morbidity occurs in over half of patients undergoing this procedure. What benefits does it offer to patients in this desperate situation? Does it produce lasting relief of symptoms, and durable local control? What is the chance of cure? To answer these questions, we will look at all the currently published reports of composite resection, beginning with Wanebo's series. His results, along with ours and 9 other surgeons, are shown in Table I. As is evident from Table I, Wanebo's experience is the most extensive, and his updated results [1] deserve careful consideration. By 1994, 53 patients had undergone composite resection of posterior or lateral pelvic recurrence of rectal cancer, 47 with curative intent and 6 for palliation. Most had previously had an anterior resection (19) or abdominoperineal resection (26), and almost all patients had already received radiotherapy in the range of 40–60 Gy. Those who had not been previously treated received chemoradiation prior to composite resection.

Of the 47 patients in whom tumor was resected with curative intent, 39 obtained microscopically clear margins. Despite gross clearance of tumor, margins were close in 6 patients and microscopically involved in 7. In the group of 47 patients who underwent curative resection, the median disease-free survival was 24 months, the median overall survival 36 months, and the 5-year disease-free survival 29%. Several factors correlated with better survival, including the type of primary operation, the original stage, and the preoperative CEA levels. Patients who had previous anterior resections, and those whose preoperative CEA levels were <10 ng/ml had a

5-year survival rate of about 45%. On the other hand, patients with previous APR or CEA levels >10 ng/ml had only 15–18% 5-year survival. The group with bone marrow invasion, positive margins, or pelvic nodal metastases had a median survival of only 10 months, comparable to the survival of the group of 6 patients who underwent resection with palliative intent.

These results suggest that well-selected patients treated with composite resection may obtain survival rates of 30% at 5 years, and 20% at 10 years. Patients who had previously had APR appeared to have a poorer prognosis for re-resection. Elevated CEA (>10 ng/ml) also predicted worse survival outcome; this might be a reflection of the fact that significant elevations of CEA usually indicate subclinical liver metastases. In addition, although it did not prove to be a statistically significant adverse factor, a very short interval to disease recurrence after primary treatment was considered by Wanebo to predict poor outcome after re-resection.

Short-term results were also reasonably favorable. Almost all patients had relief of their initial symptoms. With longer follow-up, about 30% developed secondary pain related to surgery—causalgia, sciatica, or phantom pain, but this also improved over several months. Wanebo comments that the difficulty of the procedure is reduced, and the functional result, especially bladder control, is improved when sacrectomy is limited to the S3 level. Motor deficits were generally not severe, even though half the resections in this series were carried out at the S1 level. With physiotherapy and rehabilitation, two-thirds of patients returned to their previous lifestyle and 12 of 28 returned to work.

Although Wanebo's series is the largest and has the most extensive follow-up data, several other surgeons have published their experience with sacropelvic resection. Their reports offer other insights into the technical difficulties of this complex operation, as well as its morbidity and its impact on local cancer control and survival. Our own series [57] (unpublished data) of composite resections now comprises 20 operations, most involving patients with recurrent rectal cancer. Most have already undergone previous pelvic irradiation, and if they have not, a course of radiotherapy is given prior to sacropelvic resection. In half of our patients, transection of the sacrum was carried out at the S1–S2 level, and in the remainder, at the S2–S3 level. Local control was achieved in 50% of patients at the time of death or latest follow-up. Mean and median survival times were 38 and 24 months, respectively. Two patients were alive at 12 and 15 years, giving a long-term cure rate of 10%. Effective palliation of pain was achieved in most patients and lasted until the terminal stages of their disease.

Several authors have published their experience with pelvic exenteration and included a number of composite resections. Pearlman's series [60,61] of patients undergoing extended resection of recurrent rectal cancer included 12 sacropelvic resections, with sacral transection at or below S3. Three patients were unresectable because of invasion of the proximal sacrum (S1) or tumor extension into the sciatic notch. Four of 12 patients had known extrapelvic disease, and underwent palliative resection because of severe pelvic pain. Six patients reported good postoperative relief of their cancer pain. There was 1 operative death in the group (8%). Among patients who survived the operation, 3 suffered local recurrence, and 5 died of their disease during the first year of follow-up. Two patients died without evidence of recurrence, and 3 were alive and disease-free at follow-up intervals of 6–48 months.

The 1986 report of Takagi et al. [59] includes 7 patients, all treated with composite resection for locally recurrent rectal cancer. The mean operating time was 8.8 h, and blood loss 6.2 liters; there were no operative deaths. Two patients had postoperative complications, including a perineal abscess and an intestinal fistula. All 7 patients experienced pain relief and were able to walk unaided, but only 1 patient survived, disease-free, at 22 months.

Touran et al. [62] published a series of 20 sacral resections, 9 of which were for recurrent rectal cancer, 2 for advanced primary disease, and 1 for recurrent epidermoid cancer of the anus. For this subgroup of 12 patients there were no operative deaths, the median blood loss was 1.4 liters and the median operating time 5 h for a 1-stage operation carried out with the patient in the semilateral position. Survival rates of 62% at 1 year, and 14% at 2 years were obtained. All patients had significant relief of pain postoperatively. Return of pain usually heralded a further local recurrence.

A large series from Kyoto, Japan was published by Maetani et al. [63] in 1992. Among 35 "extended" resections for recurrent rectal cancer, 23 sacral resections were included. Re-resection was not undertaken if the upper border of the tumor, as defined on MRI or CT, was above S2, or if the external iliac vessels were involved. Surprisingly, though, patients with resectable metastases to liver or lungs were included. There were 2 hospital deaths in this series. Four patients survived 5 years, but 3 of them died of a second recurrence, leaving only 1 long-term (88 month) survivor, who remained disease-free after complete pelvic exenteration and resection of the whole lower pelvic ring (inferior pelvectomy). Severe pain was relieved by surgery in 18 patients, though most complained postoperatively of numbness or dysesthesia in the denervated areas postoperatively. Ultimately, 27 of the 33 patients who recovered from surgery developed a second recurrence, mostly regional (85%), with or without distant metastases. Maetani el al. found that a longer CEA doubling time (>100 days) correlated with better overall survival. At the other end of the spectrum, pa-

tients who had distant metastases at the time of sacropelvic resection fared very badly. Based on these results, Maetani et al. concluded that extensive surgery rarely altered the outcome of locally recurrent rectal cancer, although it offered better palliation than other modalities and occasionally produced a long-term cure.

The most recent publication relating to sacropelvic resection is a 1996 article by Magrini et al. [66], in which 16 patients are described. These patients all received intraoperative electron irradiation (IOERT), along with sacropelvic resection. Fourteen had recurrent rectal cancer, previously treated with anterior resection (7) or abdominal perineal resection (APR) (7). Two had primary anal cancers, with no prior surgical treatment. All patients had a course of external beam irradiation, either at the time of their initial treatment, or immediately prior to sacropelvic resection. The surgical procedure, performed under continuous general anesthesia, consisted of four stages: an anterior approach, posterior approach, IOERT, and pelvic reconstruction. Median operative time was 12.5 h with a median blood loss of 3.4 liters. There were no operative deaths, but the rate of major complications was 50%, including perineal wound infections, dehiscence, urinary leaks and an ileal fistula. The duration of follow-up is too short to allow a meaningful assessment of cure rates, but the early results are reasonably encouraging. At a median of 18 months, 9 patients were still living, 7 without evidence of disease. Among the patients who died, 5 had distant metastases but no evidence of local failure, 1 patient died with pulmonary metastases and local recurrence, and 1 died of local disease alone. Quality of life was assessed by questionnaire in the 9 surviving patients. Eight felt that their pain was reduced and their quality of life improved after surgery. Six were able to return to their original occupation. In this group of patients whose prognosis would normally be dismal, the authors felt that sacropelvic resection, in conjunction with IOERT, provided good palliation and offered potential for cure. Combined modality therapy was generally well tolerated, although the complication rate increased with the number of intraoperative radiation fields used. Use of the rectus myocutaneous flap significantly reduced the incidence of posterior wound necrosis, which was the commonest serious complication in this and most other series.

COMBINED MODALITY THERAPY

In the management of locally recurrent rectal cancer, surgery and radiotherapy have been the mainstays of treatment. The role of chemotherapy in recurrent disease is less well defined, but has received attention lately, because of the proven usefulness of combined modality therapy in primary, locally advanced disease. A recent report from University of Texas M. D. Anderson Cancer Center [67] describes 43 patients with locally advanced recurrent rectal cancer who were treated preoperatively with concurrent external beam radiotherapy and continuous infusion of 5-fluorouracil (5-FU) or cisplatin. Intraoperative radiation or brachytherapy was used in 25 patients. All patients had initial CT evidence of contiguous involvement of pelvic viscera, sacrum, or pelvic sidewalls. At the time of surgery, 33 patients (77%) had a macroscopically complete resection, and 29 had histologically negative margins. None of these patients underwent composite resection, despite pretreatment encroachment of tumor on the bony pelvis. Fifteen patients (48%) underwent sphincter-saving operations. There were no treatment-related deaths, although perioperative complications occurred in over half of the patients. Actuarial 5-year disease-free survival for the entire group was 37%, and median survival for those who had a curative (macroscopically complete) resection was 34 months. Those results are fairly impressive, especially in comparison with the expected median survival of patients treated palliatively for locally recurrent rectal cancer, which is about 1 year. Thus, multimodality therapy seems to hold promise for improved survival and local control in this disease, and may reduce the need for sacropelvic resection and other exenterative procedures. The complication rates for combined modality therapy are higher, though. More clinical investigation is needed in this area, and the risks of therapy must be carefully weighed against the potential benefits for individual patients.

IOERT has already been mentioned as an adjunct to sacropelvic resection. Because these patients have all had previous external beam radiation, additional tumoricidal doses of radiation cannot be delivered to the whole pelvis, but must be coned down to the area at greatest risk for failure. IOERT allows for focal treatment of areas of the tumor bed that are most prone to recurrence, but it requires a dedicated operating suite or transfer of the anesthetized patient from the operating room to the radiotherapy suite. As an alternative to IOERT, brachytherapy can be used to achieve the same localized delivery of high-dose radiation to sites where there is known or suspected residual tumor after radical resection. A new approach that combines radical surgery with brachytherapy has been developed by Hockel and Knapstein [68]. Their technique, termed “combined operative and radiotherapeutic treatment” (CORT), is now used in the management of pelvic sidewall recurrences of cervical cancer, and could potentially be effective in rectal cancer as well. The procedure involves radical surgical excision of tumor, followed by the intraoperative placement of an array of silastic catheters in a parallel, single plane arrangement at the site of gross or microscopic residual tumor on the pelvic sidewall. As an essential part of the procedure, these guide tubes must then be covered with a myocutaneous flap to prevent radiation damage to adja-

cent tissues. Around day 10 postoperatively, brachytherapy is started, using an afterloading technique. Hockel and Knapstein use fractions of 6 Gy, twice weekly, to a total dose of 30–50 Gy. Using CORT, they have reported actuarial 5-year disease-free survival of 40% in this group of patients, who formerly had an extremely poor prognosis. This technique may prove to have a useful role in the treatment of rectal cancer with sacral or pelvic sidewall fixation as well. Combining brachytherapy or IOERT with radical surgery appears to reduce the risk of local relapse and improve survival in cases in which complete excision is impossible or microscopically clear margins could not be obtained. If long-term results support this benefit of combined therapy, the use of radiation, either IOERT or CORT, could alter the indications for composite resection in several ways. It might be possible to excise adherent tumor, leaving the sacrum intact and using local radiation to eradicate microscopic residual disease. Alternatively, these radiation techniques might be used to salvage composite resections in which a microscopically clear margin could not be obtained, thus expanding the usefulness of the radical surgical approach. The two modalities appear to complement one another in providing better control of fixed pelvic cancers, and more studies, with longer follow-up, will help to define their proper use in combination.

PALLIATION AS AN OUTCOME OF COMPOSITE RESECTION

The main aim of surgeons treating advanced rectal cancer with sacropelvic resection has been to salvage cure for that group of patients whose recurrent disease is confined to the pelvis. Evidence of distant metastases precludes curative surgery, and is a contraindication to composite resection, in the view of most authors. Nonetheless, there is hardly anyone who has not remarked on the palliative value of these operations. The large series of Wanebo [56] included 6 patients who were treated with palliative intent. They all presented with bulky tumors that had fistulized or ulcerated through the skin—their cancers were not only painful, but obvious, necrotic, malodorous lesions. Despite the known presence of extrapelvic disease, an effort was made to obtain clear margins locally. The median survival after composite resection in this group of patients was 8 months, with good control of pain and other symptoms. Like Wanebo et al., we have been impressed with the palliative effects of composite resection. This favorable experience has led us to offer radical surgical debridement for patients with ulcerating cancer invading the perineum. The results of such treatment have sometimes been very gratifying.

In our published series [69], 7 patients were treated, all of whom had exhausted previous treatment with radiation and chemotherapy and were admitted to hospital with unmanageable local disease. Surgery was carried out using a posterior approach in each case, with the patient positioned prone and slightly flexed. An incision was made to include a margin of about 2 cm of healthy skin and subcutaneous tissue around the visible or palpable tumor mass. The resection was then taken down through the fat of the buttocks and the gluteus maximus to the sacrum. Inferiorly the excision included sufficient tissue from the labia or scrotum to provide clear margins around the tumor. The exposed sacrum was transected above the tumor but no higher than S2–S3. Using a rongeur for this purpose helped minimize blood loss and avoid damage to the cauda equina. Tumor and sacrum were resected in continuity, but no effort was made to obtain tumor-free deep margins. Residual gross tumor was cautiously debrided using a curette or scalpel, taking care not to injure ureters, bladder, or bowel.

Finally, and crucial to the success of the operation, myocutaneous flaps were used to cover the resultant defect. By bringing healthy, unirradiated tissue with a generous blood supply into the wound, primary healing was facilitated, despite the presence of residual tumor at the base of the defect. In this series, gluteus maximus flaps were used in 6 patients and gracilis flaps in one. Now, with assistance from an experienced team of plastic surgeons, a variety of other flaps might be used, including free flaps. One patient in this group suffered necrosis of a gluteus flap, and 2 required further debridement and flap closure after tumor regrowth. All patients experienced significant pain relief. Three were able to return to work, and all patients remained at home with reasonable symptom control until the time of their death. Median survival after operation was 12 months. For patients with predominantly local disease, whose tumor has ulcerated through the skin of the perineum or buttocks, radical debulking of tumor with sacral resection offers durable palliation. The benefit in survival time is likely small, but the improvement in quality of life is dramatic; this palliative operation permits many patients to live with dignity and comfort for the remaining months of their lives.

SUMMARY

Having reviewed our experience with sacropelvic resection, we feel that this operation has a necessary place in the treatment of locally advanced rectal cancer. Experiences of Wanebo and others confirm that this admittedly radical operation can be carried out with reasonable morbidity, and with less than 10% operative mortality. Like standard pelvic exenteration, composite resection produces 5-year survival rates of 30%, and long-term cure rates between 10% and 20%. We would, however, like to emphasize that the most important contribution of surgery to the local control of rectal cancer is through precise primary excision, with careful, complete resection of the mesorectum. Adjuvant therapy has proven

advantages for local control, as well. Preoperative radiotherapy reduces local recurrence rates by half in most randomized controlled trials and clearly improves resectability of advanced lesions. Postoperative radiation is ineffective by itself, but has demonstrated benefit in both local control and survival when combined with 5-FU–based chemotherapy. Complications of postoperative chemoradiation are substantial though, and the results are still not as good as those obtained with total mesorectal excision, without any adjuvant therapy.

Despite these advances, between 5% and 20% of patients with rectal cancer will experience local recurrence. There is no doubt that extended surgery such as we have described here does have a curative and possibly a palliative role in these desperate situations. Currently, the morbidity and mortality of sacropelvic resection are not significantly different from those of pelvic exenteration, and the cure rates afforded by composite resection are only a little worse than those accepted for standard exenterative procedures. Several advances have made composite resection a safer, more effective operation. Chief among them is the use of a variety of myocutaneous flaps, particularly the rectus abdominis flap, to fill the large posterior pelvic defect. Better urinary diversion techniques have also been helpful; we prefer the Indiana pouch in most cases. Finally, the addition of local high-dose radiation, either as IOERT or brachytherapy, appears to have the potential to improve the outcome of sacropelvic resection without an excessive increase in treatment-related morbidity.

Proper selection of patients for this extensive surgery is essential. We consider that patients with extrapelvic disease are not candidates for composite resection, and we do not generally resect pulmonary or hepatic metastases in conjunction with fixed local recurrence. A very short interval to local recurrence after a good initial cancer operation is, in our experience, an indicator of biologic aggressiveness of disease, and a contraindication to extended local re-resection. We depend mainly on the CT scan to provide information about local extent of disease and technical resectability. Tumor that extends above the sacral promontory is not amenable to resection in our hands.

Finally, it is essential to have the collaboration of an experienced and committed team to obtain the best possible results. Plastic surgery and urology have critical roles to play, and radiotherapists will increasingly become involved as we begin to incorporate IOERT and brachytherapy. Postoperatively, in addition to dedicated nursing care, psychosocial support is often needed, and physiotherapy is essential in the rehabilitation of these patients. Sacropelvic resection is a demanding, radical operation, but it is the best solution to the problem of recurrent pelvic cancer with extension to the sacrum or pelvic sidewall. It reliably offers palliation of symptoms, although that should rarely be its main purpose. In a small group of patients, perhaps 10–15%, composite resection produces cure of disease. In many others, it provides months or years of good quality time before further local recurrence or distant disease leads to death. Our experience has brought home the need for better preventive strategies to reduce the incidence of local recurrence of rectal cancer, but it also supports our conclusion that radical surgery for recurrent pelvic cancer is worthwhile, even when it requires extensive procedures like sacropelvic resection.

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